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REVIEW

When to Reach for Albumin in Sepsis and Septic Shock: A Step-by-Step Reference Guide for Emergency Physicians

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Abstract

Purpose of Review To provide emergency physicians with a clear, evidence-based, and practical approach to deciding when and how to use albumin in the management of sepsis and septic shock in the emergency department (ED). This review outlines a five-step clinical framework that integrates current guidelines, trial data, and ED-specific considerations to guide albumin use in selected patient populations.

Recent Findings Crystalloids remain the first-line fluid resuscitation for sepsis, as recommended by the Surviving Sepsis Campaign (SSC). However, albumin may offer clinical benefit in cases of fluid-refractory hypotension, volume overload, hypoalbuminemia (<2.5 g/dL), septic shock with capillary leak, and in special populations such as patients with cirrhosis, nephrotic syndrome, or burns.

Summary Albumin is not a first-line resuscitation fluid, but has a role in specific ED scenarios where crystalloids alone may be insufficient or potentially harmful. A structured, stepwise framework can help emergency physicians identify when albumin may improve hemodynamics, minimize fluid overload, and support vascular integrity. Judicious use—guided by patient characteristics, response to crystalloids, and coordination with critical care teams—can enhance individualized resuscitation strategies in sepsis and septic shock. A summary of recommendations which can be utilized as a quick bedside reference is found in Table 1.

Keywords Severe sepsis · Septic shock · Continuing education · Intravenous fluids · Albumin

Introduction

Sepsis remains a major public health concern, contributing to significant morbidity, mortality, and healthcare expenditure worldwide. Between 1990 and 2017, an estimated 48.9 million global cases of sepsis resulted in approximately 11 million deaths, making it one of the leading causes of death globally [1]. In the United States alone, sepsis affects over 1.7 million adults each year and accounts for nearly 300,000 deaths annually [2]. It is consistently ranked among the costliest hospital conditions, with direct costs exceeding $24 billion in recent years [3]. These statistics highlight the critical importance of timely recognition and effective early management strategies in the emergency department (ED), where most sepsis care begins.

Historically, the management of sepsis has evolved significantly. The landmark Early Goal-Directed Therapy (EGDT) trial by Rivers et al. emphasized the importance of early intravenous fluid resuscitation, demonstrating improved survival through protocolized care within the first six hours of presentation [4]. Subsequent authors, such as Kumar et al., underscored the importance of prompt antibiotic administration, finding that each hour of delay in treatment led to a 7.6% increase in mortality [5]. These and other pivotal studies formed the foundation of contemporary sepsis management guidelines, including those established by the Surviving Sepsis Campaign (SSC).

Currently, balanced crystalloids are recommended as the first-line fluid therapy for initial resuscitation, with a

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Table 1 Summary of situations, considerations and rationales for albumin use in sepsis and septic shock

Clinical Decision Summary for Albumin Use in Sepsis and Septic Shock (ED Focus)		
Situation	Consider Albumin?	Recommendation
Septic shock after appropriate crystalloid resuscitation	Consider	*If hypotension persists despite receiving appropriate crystalloid resuscitation, albumin may be considered as an adjunctive therapy, especially in septic shock patients.*
Hypotension with signs of fluid overload	Consider	*For patients with heart failure, CKD, or cirrhosis who are prone to fluid overload, albumin may be an effective alternative to crystalloids, reducing the risk of complications like pulmonary edema.*
Serum albumin < 2.5 g/dL	Consider	*In critically ill, septic patients with hypoalbuminemia, albumin may restore oncotic pressure, improve hemodynamic stability, and enhance the pharmacokinetics of antibiotics, particularly during the early stages of resuscitation.*
Septic shock with suspected capillary leak syndrome	Consider	*In septic shock, where capillary leak compromises the effectiveness of crystalloids, albumin's higher oncotic pressure may help maintain intravascular volume and support perfusion by stabilizing the endothelial glycocalyx.*
Sepsis in cirrhosis with spontaneous bacterial peritonitis (SBP)	Consider	*Albumin is beneficial in specific populations, such as those with cirrhosis and spontaneous bacterial peritonitis, where it reduces renal failure and improves survival, as well as in nephrotic syndrome, burns, and pregnancy-related sepsis.*
Sepsis in nephrotic syndrome or burns	Consider	
Sepsis in pregnancy with preeclampsia	Consider	
Trauma or traumatic brain injury (TBI)	No	*Albumin should not be used as a first-line fluid for sepsis, nor in trauma or TBI patients, as it can worsen outcomes, and it should be avoided in hemodynamically stable, mildly septic patients or those with conditions like hypersensitivity or severe anemia, where the risks may outweigh the benefits.*
Hemodynamically stable sepsis	No	
Resource-limited setting	Consider	
Severe anemia or hypervolemia	No	
Known hypersensitivity to albumin	No	

target of 30 mL/kg in the first three hours [6]. However, not all patients respond adequately to crystalloids alone. Emerging data suggest that albumin may play a complementary role in select populations—particularly those with persistent hypotension, fluid overload, or hypoalbuminemia. For instance, the ALBIOS trial found no overall mortality benefit with albumin in sepsis, but noted improved hemodynamic stability in patients with septic shock [7]. Albumin's oncotic properties may offer advantages in patients where excessive fluid accumulation can be harmful, such as those with cirrhosis, heart failure, or chronic kidney disease.

This article offers a stepwise, bedside-focused framework for emergency physicians to determine when albumin may be a useful adjunct to crystalloid resuscitation in sepsis and septic shock. The guidance provided here synthesizes current clinical evidence, patient-specific considerations, and practical realities of emergency care, with a focus on safe, effective, and individualized fluid management. A quick-reference decision table is included to support real-time clinical application in the ED (Table 1).

Step-by-Step Clinical Framework

Step 1: Recognize the Sepsis Spectrum

Early identification of sepsis is paramount to improving outcomes. Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. In the ED, clinicians should immediately initiate evaluation and treatment in patients with suspected infection and evidence of organ dysfunction. Importantly, identifying patients who are likely to require large-volume resuscitation or who show signs of shock—such as hypotension, elevated lactate, or mental status changes—helps determine the intensity and urgency of initial interventions [8]. Early resuscitative efforts are most effective when delivered within the first hour, emphasizing the critical need for rapid recognition and triage.

Step 2: Begin Initial Fluid Resuscitation with Crystalloids

The cornerstone of early sepsis management remains timely intravenous fluid resuscitation with crystalloids. This

strategy has demonstrated benefits in restoring mean arterial pressure (MAP), improving perfusion, and enhancing lactate clearance. Clinicians should continuously monitor key indicators of response—MAP (goal≥65 mmHg), urine output (≥0.5 mL/kg/h), serum lactate, and mental status—to assess the effectiveness of initial resuscitation. With crystalloids alone, the question is raised as to whether alternative or adjunctive volume expanders, such as albumin, should be introduced.

Step 3: Consider Albumin — Who Might Benefit in the ED?

Although crystalloids are first-line, certain clinical scenarios justify consideration of albumin as an adjunct in volume resuscitation. Albumin's higher oncotic pressure allows it to remain intravascular longer than crystalloids, potentially reducing interstitial edema and improving hemodynamic status. Evidence from the ALBIOS trial found no overall mortality benefit with albumin versus crystalloids, but subgroup analysis suggested improved hemodynamics and possible benefit in patients with septic shock [7].

- **Hypotension Refractory to Initial Crystalloid Bolus**

In patients who remain hypotensive after receiving balanced crystalloids, albumin may be considered as an adjunctive fluid choice. While crystalloids are effective for initial volume expansion, they rapidly distribute into the interstitial space, which can diminish their impact on intravascular volume, especially in patients with ongoing capillary leak or vasodilation. Albumin, due to its higher oncotic pressure, remains largely within the vascular compartment and can help restore circulating volume more efficiently. The ALBIOS trial found that while 20% albumin did not reduce mortality in the overall sepsis population, patients with septic shock experienced a trend toward better outcomes, including improved hemodynamic stability and reduced vasopressor requirements [7]. Other studies also suggest that albumin may better maintain MAP and intravascular volume in shock states compared to crystalloids alone [9].

In summary: If hypotension persists despite receiving appropriatev crystalloid resuscitation, albumin may be considered as an adjunctive therapy, especially in septic shock patients.

- **Signs of Volume Overload or Fluid Intolerance**

Patients with underlying conditions such as heart failure, chronic kidney disease (CKD), or cirrhosis often exhibit limited tolerance to large volumes of crystalloid due to their predisposition to fluid overload and pulmonary edema. In these settings, additional crystalloids may exacerbate interstitial fluid accumulation, impair gas exchange, and lead to worsening respiratory failure. Albumin's oncotic properties allow for effective plasma volume expansion using smaller fluid volumes, reducing the likelihood of fluid-related complications. A large observational study in ICU patients showed that fluid overload was associated with increased mortality, particularly in patients with comorbidities affecting fluid handling [10]. Thus, in patients showing signs of elevated jugular venous pressure or radiographic evidence of pulmonary edema, albumin may offer a safer approach to resuscitation when additional volume is required.

In summary: For patients with heart failure, CKD, or cirrhosis who are prone to fluid overload, albumin may be an effective alternative to crystalloids, reducing the risk of complications like pulmonary edema.

- **Hypoalbuminemia (Serum Albumin <2.5 g/dL)**

Hypoalbuminemia is a common finding in septic patients, reflecting both inflammation-driven capillary leak and decreased hepatic synthesis. Serum albumin levels <2.5 g/dL are independently associated with increased mortality, prolonged ICU stays, and worse hemodynamic profiles in critically ill patients. Low albumin can impair vascular integrity, reduce oncotic pressure, and alter the pharmacokinetics of protein-bound drugs, including many antibiotics. Albumin replacement in this context may support intravascular volume, reduce third-spacing, and improve drug distribution—particularly important during the early phase of resuscitation when achieving therapeutic antibiotic concentrations is crucial [11]. While evidence supporting albumin use solely for hypoalbuminemia is mixed, this marker may serve as a useful adjunct in deciding whether to escalate fluid therapy beyond crystalloids.

In summary: In critically ill, septic patients with hypoalbuminemia, albumin may restore oncotic pressure, improve hemodynamic stability, and enhance the pharmacokinetics of antibiotics, particularly during the early stages of resuscitation.

- **Septic Shock with Capillary Leak Syndrome**

In the setting of septic shock, systemic inflammation and endothelial dysfunction lead to widespread capillary leak, characterized by profound vasodilation and extravasation of crystalloids into the interstitial space. This phenomenon diminishes the intravascular effectiveness of crystalloid fluids and contributes to tissue edema, hypoperfusion, and organ dysfunction. Albumin, with its larger molecular size and oncotic effect, is more likely to remain intravascular, thereby maintaining plasma volume and supporting

perfusion in patients with ongoing capillary leak. Additionally, preclinical and small human studies suggest that albumin may play a role in protecting the endothelial glycocalyx—a carbohydrate-rich layer lining the vasculature—thereby reducing vascular permeability [12]. Though this protective mechanism is still theoretical, animal models and observational human data support its plausibility, particularly in early septic shock [13].

In summary: In septic shock, where capillary leak compromises the effectiveness of crystalloids, albumin's higher oncotic pressure may help maintain intravascular volume and support perfusion by stabilizing the endothelial glycocalyx.

- **Sepsis in Special Populations**

Several patient populations may derive unique benefit from albumin due to underlying pathophysiology. In patients with cirrhosis and spontaneous bacterial peritonitis (SBP), randomized trials have shown that albumin reduces the incidence of renal failure and improves survival, making it a first-line adjunctive therapy in this context [14]. Albumin's benefits in cirrhosis are thought to stem from its ability to counteract circulatory dysfunction and prevent hepatorenal syndrome. Similarly, in nephrotic syndrome, where hypoalbuminemia and third-spacing are severe, albumin can help restore oncotic balance, though its use should be carefully weighed against risks of fluid overload. Burn patients with substantial plasma losses and pregnant patients with preeclampsia and concurrent sepsis may also benefit from albumin, although data in these populations are limited and often case-specific. These scenarios require multidisciplinary input, but albumin remains a therapeutic consideration where fluid dynamics are altered and crystalloid administration alone is suboptimal [15].

In summary: Albumin is beneficial in specific populations, such as those with cirrhosis and spontaneous bacterial peritonitis, where it reduces renal failure and improves survival, as well as in nephrotic syndrome, burns, and pregnancy-related sepsis.

Step 4: How To Administer Albumin in the ED

When albumin is indicated, proper formulation and dosing are essential. For volume resuscitation, 5% albumin is preferred due to its isooncotic properties, allowing for plasma volume expansion without creating significant osmotic shifts. The recommended initial dose is 250–500 mL IV over 30–60 min, with continuous reassessment of hemodynamics, urine output, and signs of fluid responsiveness. 25% albumin, being hyperoncotic, is generally reserved for ICU-based strategies such as diuresis in the setting of volume overload, not for initial resuscitation in the ED [16]. Repeated dosing may be necessary depending on patient response, but should be coordinated with critical care teams to avoid over-resuscitation or worsening capillary leak.

Step 5: Know when NOT To Use Albumin

Despite its potential benefits, albumin is not universally appropriate. It is not recommended as a first-line resuscitative fluid in sepsis and should not be used in trauma patients or those with traumatic brain injury, where studies have shown worse outcomes, including increased mortality in the SAFE-TBI subgroup [17]. Additionally, in hemodynamically stable patients with mild sepsis, albumin does not offer a cost-effective benefit and exposes patients to unnecessary intervention. Caution should also be exercised in resource-limited settings due to high cost, and in patients with known hypersensitivity to albumin or conditions such as severe anemia or hypervolemia, where oncotic fluid shifts may worsen clinical status. Judicious use based on patient profile, response to crystalloids, and evidence-based thresholds remains key.

Abbreviations

ED	Emergency Department
SSC	Surviving Sepsis Campaign
EGDT	Early Goal Directed Therapy
ALBIOS	Albumin in Sepsis
MAP	Mean Arterial Pressure
CKD	Chronic Kidney Disease
ICU	Intensive Care Unit
SBP	Spontaneous Bacterial Peritonitis
SAFE-TBI	Saline Versus Albumin Fluid Evaluation – Traumatic Brain Injury

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